Electroacupuncture in a rat model of early type 1 diabetes: neuroprotective action through modulation of nerve growth factor activity

Manni Luigi; Soligo Marzia; Protto Virginia

Institute of Translational Pharmacology, National Research Council of Italy (CNR), via del Fosso del Cavaliere 100, 00133, Rome, ITALY

Diabetes has been associated with dysfunctions and degeneration of basal forebrain cholinergic neurons (BFCN) that could depend upon defective nerve growth factor (NGF) utilization and incorrect activity-dependent maturation of the precursor ProNGF into mature NGF, with subsequent activation of apoptotic signaling. Electro-acupuncture (EA) could improve brain NGF availability and utilization. We hypothesized that EA could counteract the development of diabetes-associated cholinergic dysfunctions by regulating endogenous brain NGF maturation and utilization.

We used the streptozotocin (STZ) model of type 1 diabetes in young adult rats and assessed the early variations of ProNGF/NGF in the cortex and hippocampus, as well as the features of ProNGF/NGF signaling in the BFCN following STZ and EA at St36.

Four weeks after diabetes induction the ProNGF/NGF ratio was increased in the cortex and hippocampus while the pro-apoptotic c-Jun N-terminal kinase (JNK) signaling, associated with $p75^{NTR}$ receptor activation by ProNGF, was increased in the BFCN. EA counteracted the diabetes-induced deregulation of ProNGF/NGF ratio, de-activated JNK, increased tyrosine kinase-A (TrkA) receptor, Akt and extracellular signal-regulated kinases (ERK) phosphorylation.

Our data, suggesting a possible beneficial effect of EA on brain cholinergic system in diabetes, indicate that the regulation of neurotrophins' expression and activity is one of the possible neurophysiological mechanism underlying acupuncture's effects on brain neurons.

Author's e-mails:

Luigi Manni:. *luigi.manni@ift.cnr.it*

Marzia Soligo: *marzia.soligo@ift.cnr.it*

Virginia Protto: *virginia.protto@libero.it*